PATENT COOPERATION TREAT

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

A	T				
Applicant's or agent's file reference 100889-1 WO	FOR FURTHER ACTION See Form PCT/IPEA/416				
International application No.	International filing date (day/month	d/year) Priority date (day/month/year)			
PCT/SE 2003/002006	18.12.2003	20.12.2002			
International Patent Classification (IPC)	or national classification and IPC				
C07D211/58, 401/06, 4 A61P1/00, 11/00, 17/0	C07D211/58, 401/06, 401/12, 405/06, 405/12, A61K 31/4468, 31/4523, A61P1/00, 11/00, 17/00, 19/00				
Applicant					
AstraZeneca AB et al					
This report is the international pro-	eliminary examination report, establis	shed by this International Preliminary Examining			
Authority under Article 35 and tr	ansmitted to the applicant according	to Article 36.			
2. This REPORT consists of a total		this cover sheet.			
This report is also accompanied b	y ANNEXES, comprising:				
a. (sent to the applicant	and to the International Bureau) a to	otal of sheets, as follows:			
and/or sheets	sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions)				
beyond the di	sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.				
! —		type and number of electronic carrier(s))			
	, containing a sequen	ice listing and/or tables related thereto, in computer			
readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).					
4. This report contains indications re	lating to the following items:				
Box No. I Basis of	f the report				
Box No. II Priority					
Box No. III Non-esi	blishment of opinion with regard to novelty, inventive step and industrial applicability				
Box No. IV Lack of	unity of invention				
Box No. V Reasond applical	ed statement under Article 35(2) with oility; citations and explanations supp	regard to novelty, inventive step or industrial porting such statement			
Box No. VI Certain	documents cited	5 · · · · · · · · · · · · · · · · · · ·			
	defects in the international application	n			
Box No. VIII Certain	observations on the international app	lication			
Date of submission of the demand	Date of co	mpletion of this report			
	Date of w	impletion of this report			
22.06.2004		. 2005			
Name and mailing address of the IPEA/SE		Authorized officer			
Patent- och registreringsverket		- V			
Box 5055 S-102 42 STOCKHOLM		ohomes and /Tyr			
Facsimile No. +46 8 667 72 88		ohansson/EK No.+46 8 782 25 00			
Form PCT/IPEA/409 (cover sheet) (January 2004)					

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

Internal application No.
PCT/SE 2003/002006

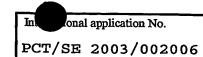
Box	k No. I	Basis of the report				
1.		regard to the language, this report is based on the international application in the language vise indicated under this item.	e in which it was filed, unless			
		This report is based on a translation from the original language into the following language which is the language of a translation furnished for the purposes of:	•			
		international search (under Rules 12.3 and 23.1(b))				
l		publication of the international application (under Rule 12.4)				
ļ		international preliminary examination (under Rules 55.2 and/or 55.3)				
2.	With regard to the elements of the international application, this report is based on (replacement sheets which have bee furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed and are not annexed to this report):					
l	\bowtie	the international application as originally filed/furnished				
	Ш	the description:				
			as originally filed/furnished			
		and the second s				
						
		the claims:				
		pages as amended (together with a	as originally filed/furnished by statement) under Article 19			
		pages* as amended (together with an pages* received by this Authority on				
		pages* received by this Authority on				
ļ		the drawings:				
		pages	as originally filed/furnished			
		pages* received by this Authority on				
		pages* received by this Authority on				
		a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence	Listing.			
3.		The amendments have resulted in the cancellation of:				
		the description, pages				
}		the claims, Nos.				
		the drawings, sheets/figs				
		the sequence listing (specify):				
		any table(s) related to the sequence listing (specify):				
4.		This report has been established as if (some of) the amendments annexed to this report made, since they have been considered to go beyond the disclosure as filed, as indicated 70.2(c)).	and listed below had not been in the Supplemental Box (Rule			
		the description, pages				
		the claims, Nos.				
		the drawings, sheets/figs				
		the sequence listing (specify):				
		any table(s) related to the sequence listing (specify):				
*	If item	4 applies, some or all of those sheets may be marked "superseded."				

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,			
	Internal application No.		
	PCT/SE 2003/002006		
	PC1/SE 2003/002006		

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability			
The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be incapplicable have not been examined in respect of:	lustrially		
the entire international application			
claims Nos. 12			
because:			
the said international application, or the said claims Nos. 12 relate to the following subject matter which does not require an international preliminary examination (specify):			
See PCT Rule 67.1.(iv).: Methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods.			
the description, claims or drawings (indicate particular elements below) or said claims Nos.			
are so unclear that no meaningful opinion could be formed (specify):			
the claims, or said claims Nos are so inadequately supby the description that no meaningful opinion could be formed.	ported		
· ·			
no international search report has been established for said claims Nos.	 ·		
the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:			
the written form has not been furnished			
does not comply with the standard			
the computer readable form has not been furnished			
does not comply with the standard the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not conthe technical requirements provided for in the Annex C-bis of the Administrative Instructions.	ıply with		
See Supplemental Box for further details.			

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Во	x No. V	Reasoned statement u citations and explanat	nder Article 3 ions supporti	5(2) with regard to novelty, inventive step or industrial applicabilitying such statement	у;
1.	Statement				
	Novel	ty (N)	Claims Claims	1-11	YES NO
	Invent	tive step (IS)	Claims Claims	1-11	YES NO
	Indust	rial applicability (IA)	Claims Claims	1-11	YES NO

2. Citations and explanations (Rule 70.7)

The following documents are cited in the search report:

D1 WO 0187839 A1

D2 WO 0076514 A1

D3 WO 9202502 A1

D4 EP 903349 A2

D5 WO 0192227 A1

The claimed invention relates to novel piperidine derivatives, which act as modulators of chemokine receptor activity, especially CCR5.

D1 discloses structurally close piperidine derivatives, which act as modulators of chemokine receptor activity, especially CCR5.

The novel piperidine derivatives differ from D1 only in that an unbroken carbon-chain is bound to a carbon atom in the piperidine-ring, while in the known compounds an -N-X-chain where X is e.g. a bond is bound to a carbon atom in the piperidine-ring in the same way. The remaining substitutions in the structure are the same.

D2 discloses structurally close piperidine derivatives, which act as modulators of chemokine receptor activity, especially CCR5.

The novel piperidine derivatives differ from D2 mainly in the substitution on the nitrogen-atom in the piperidine-ring. The carbon-chain, which is bound to a carbon-atom in the piperidine-ring, could be the same as X in D2, when X is -(C

.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient. Continuation of: BOX V

0-6 alkyl)-Y-(C 0-6 alkyl)- and Y is a bond.

The compounds in D1 and D2 have the same therapeutical use as the known and thus solve the same problem as the known compounds.

In the light of the prior art and having regarded the present description and claims, the problem underlying the present application is to find further compounds which act as modulators of chemokine receptor activity, especially CCR5.

The solution proposed in claims 1-11 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons.

It is common practice to synthesise analogues of known compounds. In the present case, D1 as well as this application, may serve as examples.

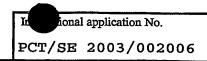
The selected novel compounds must show an unexpected and advantageous effect over the prior art. No such effect has been demonstrated for the present compounds. In the absence of relevant biological activity data to the support of the compounds, no inventive step can be acknowledged for the entire scope of the claims. The basis for recognition of inventive step of the present compounds over the closest prior art might lie in the assessment that, particularly in the realm of biologically active compounds, even small structural modifications may cause dramatic changes in activity.

However, the structural differences between the compounds of the prior art D1 and the present compounds are at least as great as the structural differences between the latter compounds and the present, structurally more remote compounds.

Thus, the claims 1-11 are novel but lack inventive step. The claims have industrial applicability.

D3-D5 disclose the general state of the art and are not considered to be particular relevant.

INTERNATIONAL PRED. MARY REPORT ON PATENTABILITY



Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1-3, partly 4-7 and 8-11 are not supported by the description as required by Article 6 PCT, as their scope is broader than justified by the description and drawings. The reasons therefore are the following: The examples show only two kinds of structures (table I and example 1 and 2).